REMARKS

Claims 2 and 4-34 are currently pending in the application. Claims 2, 4 and 11-16 are currently under examination. Claims 1, 3, and 35 are canceled. Claims 2, 4, 11, 13 and 14 are amended. Claim 36 is new. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

The Office Action states at page 8, lines 10-12, that a protein consisting of amino acids 1-175 of SEQ ID NO:2 is free of the prior art, the specification shows that this protein has anti-angiogenic activity, and thus is allowable subject matter. New claim 36 recites such a protein.

Rejection of Claim 35 Under 35 U.S.C. § 112, First Paragraph

Claim 35 remains rejected under 35 U.S.C. § 112, first paragraph, for failure to comply with the enablement requirement. Although Applicant does not acquiesce to this rejection, claim 35 has been cancelled, thereby obviating the rejection.

Objection to the Specification

The disclosure has been objected to because it contains an embedded hyperlink. The Applicant has amended the specification to remove the embedded hyperlink, thereby obviating the objection.

The Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 2-4 and 11-16 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office Action states that claim 2 is confusing for several reasons. First, claim 2 is said to be confusing in the use of open language ("comprises") in reference to the amino acid sequence of EM 1, since the specification states that the EM 1 protein is SEQ ID NO:2. The Office Action states that the open language "comprising" a mutant causes the claim to read on

the known full-length endostatin protein. Second, it is not clear whether the various occurrences of "endostatin protein" refer to the same or different proteins. Third, the claim is unclear as to what is being deleted, as well as the meanings of "mutated endostatin protein" and "EM 1." Finally, there is insufficient antecedent basis for the term "mutation" in line 2.

Applicant appreciates the Examiner's comments and for noting the potentially ambiguous and indefinite language of claim 2. In response, Applicant has rewritten claim 2 to (1) eliminate the potentially confusing terms (i.e., "comprises," "mutated endostatin protein," and "EM 1"); (2) eliminate duplicative use of the term "endostatin protein"; and (3) provide proper antecedent basis for the term "deletion mutation." Claim 2 as amended now recites the closed transitional language "consisting of" in reference to the deletion mutation. Moreover, as amended, claim 2 recites a specific amino acid sequence of SEQ ID NO:2. Specifically, claim 2 as now written requires that the anti-angiogenic polypeptide comprise residues 168-175 of the endostatin protein of SEQ ID NO:2. Claim 2 also incorporates the limitations of dependent claim 3 (now cancelled), which recites the specific deletion mutation (i.e., the 9 amino acid sequence of SEQ ID NO:24). As is stated throughout the disclosure, Applicant discovered that EM 1, a truncated version of endostatin, has the surprising ability to inhibit angiogenesis despite lacking the nine consecutive amino acids at the C-terminus of endostatin (see, e.g., pages 9 and 10, Example 12, and Figure 20). Moreover, and importantly, Applicant discovered the *active site* of the endostatin mutant responsible for the anti-angiogenic activity. Whereas EM 1 (which contains amino acid residues 168-175 of SEQ ID NO:2) has strong angiogenesis inhibitory activity, another mutant, EM 2, which differs by only eight amino acids (i.e., EM 2 lacks residues 168-175), lacks this inhibitory activity. Thus, in addition to clarifying the metes and bounds of the invention, claim 2 as amended specifically requires the active site sequence, i.e., amino acids 168-175 of SEQ ID NO:2.

Because claim 2 as amended incorporates the limitations of dependent claim 3, claim 3 has been cancelled, and claims 11 and 13, which previously depended from claim 3, have been amended to depend from amended claim 2.

The Office Action states that claim 11 is confusing because it is not clear whether all of the protein molecules are present as a single polypeptide in the fusion protein. Applicant believes that the amendments to claim 11 remove the confusing language, and that the claim as rewritten is clear and unambiguous.

Applicant believes that the above-discussed amendments to claims 2 and 11 obviate the rejections under 35 U.S.C. § 112, second paragraph, and respectfully request reconsideration and withdrawal of the rejections.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 2-5, 11-16, and 35 have been ejected under 35 U.S.C. § 112, first paragraph, for failure to comply with the written description requirement. The Office Action states that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The rejection is based on the assumption that while EM1 has the unexpected property of having anti-angiogenic activity, EM 1 as defined in the specification includes a large number of "unpredictable species (the entire mammalian species)," and that the specification "does not teach the structure" of the molecule responsible for this activity (paragraph bridging pages 5 and 6 of the Office Action).

As discussed above, Applicant discovered that a deletion mutant of endostatin (EM 1) has the surprising ability to inhibit angiogenesis despite lacking the nine consecutive amino acids at the C-terminus of endostatin (see, e.g., pages 9 and 10, Example 12, and Figure 20). Moreover, and importantly, Applicant discovered the *active site* of the endostatin mutant responsible for the anti-angiogenic activity, namely amino acid residues 168-175 of SEQ ID NO:2. Thus, any polypeptide comprising the recited active site sequence would be expected to have the claimed anti-angiogenic activity.

Although not acquiescing to this rejection, Applicant has rewritten claim 2 to specifically recite the structure responsible for the surprising biological activity of EM 1, i.e., the active site sequence, amino acids 168-175 of SEQ ID NO:2.

The fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date, applicant was in possession of the claimed invention. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 19 U.S.P.Q.2d 1111, 1117 (Fed. Cir. 1991). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patent" such as by the disclosure of drawings or structural information that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Electronics, Inc.*, 48 U.S.P.Q.2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly*, 43 U.S.P.Q.2d 1398, 1405 (Fed. Cir. 1997) ("written description of an invention involving a chemical genus . . . 'requires a precise definition, such as by structure, formula, [or] chemical name"). As discussed above, Applicant has provided the "distinguishing identifying characteristics" or structural features common to the claimed polypeptides having anti-angiogenic activity. The specification discloses the structure-function relationship responsible for this unexpected property, and the claims as amended recite the common structural feature (i.e., amino acids 168-175 of SEQ ID NO:2) associated with the surprising anti-angiogenic activity.

Applicant believes that the above-discussed amendments to claim 2 obviate the rejection of claims 2-5 and 11-16 under 35 U.S.C. § 112, first paragraph, and respectfully request reconsideration and withdrawal of the rejection.

Rejections Under 35 U.S.C. § 102

Claims 2-4, 11, and 13-15 have been ejected under 35 U.S.C. § 102 as being anticipated by O'Reilly et al. (*Cell*, 88:277-285, Jan. 1997), as evidenced by Oh et al. (*Proc. Natl. Sci. Acad. USA*, 91:4229-33, 1994), "for the C-terminal 20 kDa fragment sequence information of the collagen type XVIII." The Office Action states the "[t]his rejection is based on the Office's interpretation that the limitation "comprising" in line 1 of claim 2 controls the scope of the claimed invention. The claims as written read on the recombinant endostatin fusion protein of O'Reilly et al." (paragraph bridging pages 6 and 7).

Applicant has amended claim 2 to eliminate the open terminology ("comprising"), and to clarify that the anti-angiogenic polypeptide lacks the nine consecutive amino acids from the C-terminus of the endostatin protein, thereby obviating the rejection.

Claims 2-4, 12-16, and 35 have been ejected under 35 U.S.C. § 102 as being anticipated by O'Reilly et al. (U.S. Pat. No. 5,854,205), as evidenced by Oh et al. (*Proc. Natl. Sci. Acad. USA*, 91:4229-33, 1994), "for the C-terminal 20 kDa fragment sequence information of the collagen type XVIII." The Office Action states the "[t]he rejection is based on the Office's interpretation that the limitation "comprising" in line 1 of the base claim controls the scope of the claims 2-4, and 12-16. See the rejection under 102 (a) above."

Again, Applicant has amended claim 2 to eliminate the open terminology ("comprising"), and to clarify that the anti-angiogenic polypeptide lacks the nine consecutive amino acids from the C-terminus of the endostatin protein, thereby obviating the rejection.

Claim 35 was rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Pat. No. 6,080,728. Claim 35 has been cancelled, thereby obviating this rejection.

Applicant believes that the foregoing amendment obviates the rejection of claims 2-4 and 11-16 under 35 U.S.C. § 102, and respectfully requests reconsideration and withdrawal of the rejections.

Applicant submits that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicant's attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record.

Respectfully submitted,

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